



PTO/SB/21 (08-03)

Approved for use through 08/30/2003. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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TRANSMITTAL FORM (to be used for all correspondence after initial filing)	Application Number	10/789,308	
	Filing Date	02/26/04	
	First Named Inventor	Thomas M. Jessell	
	Art Unit	1636	
	Examiner Name	to be assigned	
Total Number of Pages in This Submission	28	Attorney Docket Number	5199-152

ENCLOSURES (Check all that apply)		
<input type="checkbox"/> Fee Transmittal Form <input type="checkbox"/> Fee Attached <input type="checkbox"/> Amendment/Reply <input type="checkbox"/> After Final <input type="checkbox"/> Affidavits/declaration(s) <input type="checkbox"/> Extension of Time Request <input type="checkbox"/> Express Abandonment Request <input checked="" type="checkbox"/> Information Disclosure Statement <input type="checkbox"/> Certified Copy of Priority Document(s) <input type="checkbox"/> Response to Missing Parts/Incomplete Application <input type="checkbox"/> Response to Missing Parts under 37 CFR 1.52 or 1.53	<input type="checkbox"/> Drawing(s) <input type="checkbox"/> Licensing-related Papers <input type="checkbox"/> Petition <input type="checkbox"/> Petition to Convert to a Provisional Application <input type="checkbox"/> Power of Attorney, Revocation Change of Correspondence Address <input type="checkbox"/> Terminal Disclaimer <input type="checkbox"/> Request for Refund <input type="checkbox"/> CD, Number of CD(s) _____	<input type="checkbox"/> After Allowance communication to Technology Center (TC) <input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences <input type="checkbox"/> Appeal Communication to TC (Appeal Notice, Brief, Reply Brief) <input type="checkbox"/> Proprietary Information <input type="checkbox"/> Status Letter <input checked="" type="checkbox"/> Other Enclosure(s) (please Identify below): Return receipt postcard
Remarks		
SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT		
Firm or Individual name	Todd Holmbo, Reg. No. 42,665	
Signature		
Date	11/24/04	

CERTIFICATE OF TRANSMISSION/MAILING			
I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below.			
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Thomas Jessel, et al. Docket No.: 5199-152
Serial No.: 10/789,308 Examiner: to be assigned
Filed: February 26, 2004 Group Art Unit: 1636
Title: **SYSTEMS AND METHODS FOR SCREENING FOR
MODULATORS OF NEURAL DIFFERENTIATION**

November 24, 2004

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

INFORMATION DISCLOSURE STATEMENT
UNDER 37 CFR §1.97(b)

Sir:

In accordance with the duty of disclosure under 37 CFR §1.56, applicant hereby notifies the U. S. Patent and Trademark Office of the following documents, which are listed on the attached PTO/SB/08B form. The examiner may deem these documents to be relevant to patentability of the claims of the above-identified application. Copies of the documents are enclosed for the examiner's convenience.

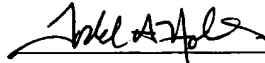
The submission of the listed documents is not intended as an admission that any of the documents constitute prior art against the claims of the present application. Applicants do not waive any right to take any action that would be appropriate to antedate or otherwise remove any listed document as a competent reference against the claims of the present application.

Applicants respectfully request that the listed documents be considered by the examiner and be made of record in the present application and that an initialed copy of Form PTO/SB/08B be returned in accordance with MPEP §609.

It is understood that no fee is necessary for submission of this Information Disclosure Statement, because it is being filed before the later of three months from the filing date or the mailing of the first Office Action on the merits.

The Commissioner is hereby authorized to charge payment of any fees associated with this application or credit any overpayment to Deposit Account No. 02-4270.

Respectfully submitted,



Todd Holmbo

Reg. No. 42,665

Attorney for Applicants

BROWN RAYSMAN MILLSTEIN

FELDER & STEINER LLP

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PTO/SB/08B (08-03)

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Substitute for form 1449/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Complete if Known

Application Number 10/789,308

Filing Date 02/26/04

First Named Inventor Thomas M. Jessell

Art Unit 1636

Examiner Name to be assigned

Attorney Docket Number 5199-152

Sheet 1 of 25

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
		Abbondanzo et al., Derivation of embryonic stem cell lines.	
		Methods Enzymol., 225: 803-823, 1993	
		Akhurst and Derynck, TGF-beta signaling in cancer-a double-edged sword.	
		Trends Cell Biol., 11(11): S44-51, 2001	
		Alvarez-Buylla et al., A unified hypothesis on the lineage of neural stem cells.	
		Nat. Rev. Neurosci., 2: 287-293, 2001	
		Arber et al., Requirement for the homeobox gene Hb9 in the consolidation of motor neuron identity.	
		Neuron, 23: 659-764, 1999	
		Bain et al., Embryonic stem cells express neuronal properties in vitro.	
		Dev. Biol., 168: 342-357, 1995	

Examiner Signature	Date Considered
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*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO:

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		Art Unit	1636
		Examiner Name	to be assigned
Sheet 2 of 25	Attorney Docket Number	5199-152	

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		Bak et al., The Hedgehog signaling pathway – implications for drug targets in cancer and neurodegenerative disorders.	
		Pharmacogenomics, 4(4): 411-429, 2003 (N/A)	
		Beers and Berkow, eds., The Merck Manual of Diagnosis and Therapy, 17th ed. Whitehouse Station, NJ: Merck Research Laboratories, 1999, chap. 183	
		Belting et al., Multiple phases of expression and regulation of mouse Hoxc8 during early embryogenesis.	
		J. Exp. Zool., 282: 196-222, 1998	
		Bieri et al., Abnormal nerve conduction studies in mice expressing a mutant form of the POU transcription factor, SCIP.	
		J. Neurosci. Res., 50:821-828, 1997	
		Bloch-Gallego et al., Survival in vitro of motoneurons identified or purified by novel antibody-based methods is selectively enhanced by	
		muscle-derived factors.	
		Development, 111: 221-232, 1991	

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Sheet 3 of 25	Attorney Docket Number	5199-152	

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		Blumberg et al., An essential role for retinoid signaling in anteroposterior neural patterning.	
		Development, 124: 373-379, 1997	
		Botchkarev, V.A., Bone morphogenetic proteins and their antagonists in skin and hair follicle biology.	
		Journal of Investigative Dermatology, 120: 36-47, 2003	
		Brazelton et al., From marrow to brain: expression of neuronal phenotypes in adult mice.	
		Science, 290: 1775-1779, 2000	
		Briscoe and Ericson, Specification of neuronal fates in the ventral neural tube.	
		Curr. Opin. Neurobiol., 11: 43-49, 2001	
		Briscoe et al., A homeodomain protein code specifies progenitor cell identity and neuronal fate in the ventral neural tube.	
		Cell, 101: 435-445, 2000	

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		Art Unit	1636
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Sheet 4	of 25	Attorney Docket Number	5199-152

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		Byrd et al., Hedgehog is required for murine yolk sac angiogenesis.	
		Development, 129: 361-372, 2002	
		Cadigan and Nusse, Wnt signaling: a common theme in animal development.	
		Genes Dev., 11(24): 3286-3305, 1997	
		Camu et al., Purification of embryonic rat motoneurons by panning on a monoclonal antibody to the low-affinity NGF receptor.	
		J. Neurosci. Methods, 44: 59-70, 1992	
		Chambon, P., The molecular and genetic dissection of the retinoid signaling pathway.	
		Recent Prog. Horm. Res., 50: 317-332, 1995	
		Chambon, P., The retinoid signaling pathway: molecular and genetic analysis.	
		Semin. Cell Biol., 5(2): 115-125, 1994	

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		Art Unit	1636
		Examiner Name	to be assigned
Sheet 5	of 25	Attorney Docket Number	5199-152

NON PATENT LITERATURE DOCUMENTS			
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		Chiang et al., Cyclopia and defective axial patterning in mice lacking Sonic hedgehog gene function.	
		Nature, 383: 407-413, 1996	
		Chiba et al., Distinct retinoid X receptor – retinoic acid receptor heterodimers are differentially involved in the control of expression of	
		of retinoid target genes in F9 embryonal carcinoma cells.	
		Mol. Cell Biol., 17: 3013-3020, 1997	
		Choi et al., A generic intron increases gene expression in transgenic mice.	
		Mol. Cell Biol., 11: 3070-3074, 1991	
		Cross and Claesson-Welsh, FGF and VEGF function in angiogenesis: signaling pathways, biological responses and therapeutic inhibition.	
		Trends Pharmacol. Sci., 22(4): 201-207, 2001	

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Substitute for form 1449/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Complete if Known

Application Number 10/789,308

Filing Date 02/26/04

First Named Inventor Thomas M. Jessell

Art Unit 1636

Examiner Name to be assigned

Attorney Docket Number 5199-152

Sheet 6

of 25

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
		Danielsen and Maihle, The EGF/ErbB receptor family and apoptosis.	
		Growth Factors, 20(1): 1-15, 2002	
		Davis and Joyner, Expression patterns of the homeobox-containing genes En-1 and En-2 and the proto-oncogene int-1 diverge during mouse development.	
		Genes Dev., 2: 1736-1744, 1988	
		Durst et al., Retinoids and related signals in early development of the vertebrate central nervous system.	
		Curr. Top. Dev. Biol., 40: 111-175, 1998 (N/A)	
		Dyer et al., Indian hedgehog activities hematopoiesis and vasculogenesis and can respecify prospective neurectodermal cell fate in the mouse embryo.	
		Development, 128: 1717-1730, 2001	

Examiner
SignatureDate
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Sheet	7	of	25	Attorney Docket Number	5199-152

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		Ericson et al., Pax6 controls progenitor cell identity and neuronal fate in response to graded SHh signaling.	
		Cell, 90: 169-180, 1997	
		Ericson et al., Two critical periods of Sonic Hedgehog signaling required for the specification of motor neuron identity.	
		Cell, 87: 661-673, 1996	
		Falls, D.L., Neuregulins: functions, forms, and signaling strategies.	
		Exp. Cell Res., 284(1) 14-30, 2003	
		Frank-Kamenetsky et al., Small-molecule modulators of Hedgehog signaling: Identification and characterization of Smoothed agonists and antagonists.	
		J. Biol. 1(2): 10, 2002	
		Gage, F. H., Mammalian neural stem cells.	
		Science, 287: 1433-1438, 2000	

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Sheet 8	of 25	Attorney Docket Number	5199-152

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		Giles et al., Caught up in a Wnt storm: Wnt signaling in cancer.	
		Biochim. Biophys. Acta., 1653(1): 1-24, 2003	
		Goodwin and D'Amore, Wnt signaling in the vasculature.	
		Angiogenesis, 5(1-2): 1-9, 2002 (N/A)	
		Gratsch et al., Noggin and chordin have distinct activities in promoting lineage commitment of mouse embryonic stem (ES) cells.	
		Dev. Biol., 245: 83-94, 2002 (N/A)	
		Hatsell et al., Beta-catenin and Tcfs in mammary development and cancer.	
		J. Mammary Gland Biol. Neoplasia., 8: 145-158, 2003	
		Hollyday et al., An autoradiographic study of the formation of the lateral motor column in the chick embryo.	
		Brain Res., 132: 197-208, 1977	

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		Filing Date	02/26/04		
		First Named Inventor	Thomas M. Jessell		
		Art Unit	1636		
		Examiner Name	to be assigned		
Sheet	9	of	25	Attorney Docket Number	5199-152

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
		Hsieh et al., Biochemical characterization of Wnt-frizzled interactions using a soluble, biologically active vertebrate Wnt protein.	
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		Lauta, V. M., A review of the cytokine network in multiple myeloma: diagnostic, prognostic, and therapeutic implications.	
		Cancer, 97(10): 2440-2452, 2003	
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		Lee et al., Efficient generation of midbrain and hindbrain neurons from mouse embryonic stem cells.	
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		Lu et al., Common developmental requirement for Olig function indicates a motor neuron/oligodendrocyte connection.	
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		Mezey et al., Turning blood into brain: cells bearing neuronal antigens generated in vivo from bone marrow.	
		Science, 290: 1779-1782, 2000	

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		Miyazono et al., Divergence and convergence of TGF-beta/BMP signaling.	
		J. Cell Physiol., 187(3): 265-276, 2001	
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		Moon et al., The promise and perils of Wnt signaling through beta-catenin.	
		Science, 296(5573): 1644-1646, 2002	

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		Muhr et al., Convergent inductive signals specify midbrain, hindbrain, and spinal cord identity in gastrula stage chick embryos.	
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		Novitch et al., Coordinate regulation of motor neuron subtype identity and pan-neuronal properties by the bHLH repressor Olig2.	
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		Development, 130(22): 5297-5305, 2003	

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		O'Brien et al., Development and survival of thoracic motoneurons and hindlimb musculature following transplantation of the thoracic neural tube	
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		Pattyn et al., Control of hindbrain motor neuron differentiation by the homeobox gene Phox2b.	
		Development, 127: 1349-1358, 2000	

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		Pevny et al., Generation of purified neural precursors from embryonic stem cells by lineage selection.	
		Curr. Biol., 8: 971-974, 1998	
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		Nat. Cell Biol., 4(11): E249-250, 2002	

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		Raju et al., SANE, a novel lem domain protein, regulates bone morphogenetic protein signaling through interaction with smad1.	
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		Ring and Cho, Specificity in transforming growth factor- <i>beta</i> signaling pathways.	
		Am. J. Hum. Genet., 64: 691-697, 1999	

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		Roelink et al., Floor plate and motor neuron induction by different concentrations of the amino-terminal cleavage product of sonic hedgehog	
		autoproteolysis.	
		Cell, 81: 445-455, 1995	
		Sander et al., Ventral neural patterning by Nkx homeobox genes: Nkx6.1 controls somatic motor neuron and ventral interneuron fates.	
		Genes Dev., 14: 2134-2139, 2000	
		Schuldiner et al., Induced neuronal differentiation of human embryonic stem cells.	
		Brain Res., 913: 201-205, 2001	
		Sharma et al., Genetic and epigenetic mechanisms contribute to motor neuron pathfinding.	
		Nature, 406: 515-519, 2000	

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		Art Unit	1636
		Examiner Name	to be assigned
Sheet 19 of 25	Attorney Docket Number	5199-152	

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
		Sharma et al., LIM homeodomain factors Lhx3 and Lhx4 assign subtype identities for motor neurons.	
		Cell, 95: 817-828, 1998	
		Shibamoto et al., Cytoskeletal reorganization by soluble Wnt-3a protein signaling.	
		Genes Cells, 3: 659-670, 1998	
		Streit et al., Initiation of neural induction by FGF signaling before gastrulation.	
		Nature, 406: 74-78, 2000	
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		Temple, S., The development of neural stem cells.	
		Nature, 414:112-117, 2001	

Examiner Signature		Date Considered	
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use as many sheets as necessary)		Complete if Known	
		Application Number	10/789,308
		Filing Date	02/26/04
		First Named Inventor	Thomas M. Jessell
		Art Unit	1636
		Examiner Name	to be assigned
Sheet 20 of 25	Attorney Docket Number	5199-152	

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		Terada et al., Bone marrow cells adopt the phenotype of other cells by spontaneous cell fusion.	
		Nature, 416: 542-545, 2002	
		Thaler et al., Active suppression of interneuron programs within developing motor neurons revealed by analysis of homeodomain factor HB9.	
		Neuron, 23: 675-687, 1999	
		Tropepe et al., Direct neural fate specification from embryonic stem cells: a primitive mammalian neural stem cell stage acquired through a default	
		mechanism.	
		Neuron, 30: 65-78, 2001	
		Tsuchida et al., Topographic organization of embryonic motor neurons defined by expression of LIM homeobox genes.	
		Cell, 79: 957-970, 1994	

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		Uchida et al., Direct isolation of human central nervous system stem cells.	
		Proc. Natl. Acad. Sci. USA, 97: 14720-14725, 2000	
		Vallstedt et al., Different levels of repressor activity assign redundant and specific roles to NKx6 genes in motor neuron and interneuron specification.	
		Neuron, 31: 743-755, 2001	
		Van Es et al., You Wnt some, you lose some: oncogenes in the Wnt signaling pathway.	
		Curr. Opin. Genet. Dev., 13(1): 28-33, 2003	
		Van Gijn et al., The Wnt-frizzled cascade in cardiovascular disease.	
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		Veeman et al., A second canon: functions and mechanisms of beta-catenin-independent Wnt signaling.	
		Dev. Cell 5(3): 367-377, 2003	

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		Application Number	10/789,308
		Filing Date	02/26/04
		First Named Inventor	Thomas M. Jessell
		Art Unit	1636
		Examiner Name	to be assigned
Sheet 22 of 25	Attorney Docket Number	5199-152	

NON PATENT LITERATURE DOCUMENTS			
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		Waxman and Bennett, Relative conduction velocities of small myelinated and nonmyelinated fibres in the central nervous system.	
		Nature New Biol., 238:217, 1972	
		Weston et al., Revisiting the role of retinoid signaling in skeletal development.	
		Birth Defects Res. Part C Embryo Today, 69(2): 156-173, 2003	
		Wetmore, C., Sonic hedgehog in normal and neoplastic proliferation: insight gained from human tumors and animal models.	
		Curr. Opin. Genet. Dev., 13(1): 34-42, 2003	
		Wilson et al., Neural induction: toward a unifying mechanism.	
		Nat. Neurosci., 4th Suppl.: 1161-1168, 2001	
		Wilson et al., An early requirement for FGF signaling in the acquisition of neural cell fate in the chick embryo.	
		Curr. Biol., 10: 421- 429, 2000	

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		Art Unit	1636
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		Wilson et al., The status of Wnt signaling regulates neural and epidermal fates in the chick embryo.	
		Nature, 411: 325-330, 2001	
		Wodarz and Nusse, Mechanisms of Wnt signaling in development.	
		Annu. Rev. Cell Dev. Biol., 14: 59-88, 1998	
		Wood et al., Comparative expression of the mouse Sox1, Sox2 and Sox3 genes from pre-gastrulation to early somite stages.	
		Mech. Dev., 86: 197-201, 1999	
		Wrana, J., Regulation of Smad activity.	
		Cell, 100: 189-192, 2000	
		Xian et al., Peering into early neurogenesis with embryonic stem cells.	
		Trends Neurosci., 24: 685-686, 2001	

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		Art Unit	1636
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		Yamada et al., Control of cell pattern in the developing nervous system: polarizing activity of the floor plate and notochord.	
		Cell, 64: 635-647, 1991	
		Yamaguchi et al., XIAP, a cellular member of the inhibitor of apoptosis protein family, links the receptors to TAB1-TAK1 in the BMP signaling pathway.	
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		Ying et al., Changing potency by spontaneous fusion.	
		Nature, 416: 545-548, 2002	
		Yu et al., Platelet-derived growth factor signaling and human cancer.	
		J. Biochem. Mol. Biol., 36(1): 49-59, 2003	
		Zhang et al., In vitro differentiation of transplantable neural precursors from human embryonic stem cells.	
		Nat. Biotechnol., 19: 1129-1133, 2001	

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**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Complete if Known

Application Number 10/789,308

Filing Date 02/26/04

First Named Inventor Thomas M. Jessell

Art Unit 1636

Examiner Name to be assigned

Attorney Docket Number 5199-152

Sheet

25

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		Zhou et al., The bHLH transcription factors OLIG2 and OLIG1 couple neuronal and glial subtype specification.	
		Cell, 109: 61-73, 2002	

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